REMARKS

Claims

Claims 1–3 and 9–15 are currently under examination

Claims 4–8 withdrawn from consideration due to restriction/election pursuant to the Restriction Requirement mailed June 18, 2008.

Claim amendments

Support for the amendment of the claims can be found in, for example, the first complete paragraph in page 6, paragraph 1 and the disclosure contained in page 12 of the originally-filed specification.

It is respectfully submitted that the claim amendments do not raise new matter. Entry thereof is earnestly solicited.

Specification

The specification has been amended to include a brief description of the drawings section. Withdrawal of the objection is respectfully requested.

Sequence listing

A revised sequence listing, along with an amendment in the specification to recite the sequence identifier numbers (SEQ ID NO) of the sequences recited therein, is submitted herewith. No new matter is added. Entry thereof is respectfully requested.

Claim objections

Claims 3 and 9 are objected to for allegedly reciting non-elected inventions. At page 3, the Office Action alleges that the claimed aspect "providing a nuclear factor which is capable of functionally coupling the Rev-erb to an RNA-polymerase complex, and measuring the binding **[of test substance] to a nuclear factor capable** of functionally coupling said hRev-erb to the RNA polymerase complex" is directed to non-elected subject matter. Applicants respectfully disagree with this contention. Firstly, it is submitted that the Examiner's interpretation that the test substance binds to a nuclear factor is incorrect. The claimed method invovles measuring the binding of the "test substance-hRev-erb receptor complex" to the hRev-erb response element and/or to the nuclear factor. Secondly, the objected claims involve essentially all the method steps of the examined claim 1, and recite additional method steps that might be included in the screening assays. As such, it would not constitute undue burden on the PTO to examine the subject matter of these claims.

See, MPEP §803. Favorable action is earnestly solicited.

Applicants thank the Examiner for her careful review of claim 11. The foregoing amendments render the objection moot.

Withdrawal of the claim objections is respectfully requested.

Finality of the rejection

The Office Action relies on a newly cited Harding et al. reference to reject all the claims of the present application. It is not clear whether the finality of the rejection was necessitated by Applicants amendments filed December 11, 2008. Applicants respectfully submit that in line with the provisions set forth under MPEP §706.07, the finality of the rejection should be withdrawn.

Rejection under §112, ¶2

The foregoing amendments render the rejection of claims 9, 12, and 13 under this section moot. No agreement is to be implied.

Applicants therefore respectfully submit that the claim language is sufficiently definite, especially in the context of Applicants' instant specification and the information available to the skilled worker prior to the filing of the instant application. Withdrawal of the rejection is respectfully requested.

Rejection under §103

Claims 1, 3 and 9 are rejected under §103(a) as allegedly rendered obvious by Trueheart (US patent No.: 6,159,705; the '705 patent) in view of Harding (*Molecular and Cellular Biology*, 1995) and vu-Dac et al (*JBC*, 1998). Claim 2 is rejected under this section as allegedly unpatentable over Trueheart and Harding, further in view of Adelmant (*Proceedings of the National Academy of Sciences*, 1996). Claims 10–13 are rejected under the same section as allegedly rendered obvious by Trueheart and Harding further in view of vu-Dac, Fraser (*JBC*, 1997) and Auwerx (*Atherosclerosis*, 1996). Claims 14 and 15 are rejected under this section as allegedly unpatentable over the aforementioned Trueheart, Harding, vu-Dac references, further in view of Terenzi (*Protein Expression and Purification*, 1996). Applicants respectfully traverse these rejections.

The limitations of the primary Trueheart reference have been outlined in Applicants' response filed December 11, 2008. Trueheart does not teach or suggest screening techniques involving *human Rev-erb* of the present invention and more specifically, human Rev-erbα as disclosed in the present application. With respect to the generic disclosure of nuclear receptors, Trueheart proceeds to disclose a number of steroid hormone and thyroid hormone responsive transcriptional

control units. Trueheart is absolutely silent with respect to human Rev-erb response elements, as claimed herein. These limitations were conceded by the Examiner at page 12 of the Office Action, wherein it is stated that "the response elements were not further identified" by Trueheart. The Office Action contends that the missing claimed elements are taught in Harding. Applicants respectfully disagree with this contention.

Harding teaches that direct repeats (DR) AGGTCA sequence serve as a binding site for Rev-erb. The Examiner proceeds to contends that a skilled worker would have been motivated to use such consensus DNA motifs with Trueheart's screening techniques. Applicants respectfully disagree. Trueheart generically teaches that "at least four groups of orphan nuclear receptors represented by NGF1, FTZ-F1, Rev-erbs, and RARs, which are by evolutionary standards, only distantly related to each other...bind to a palindrome of their hormone responsive element." However, Trueheart does not teach or suggest that the binding of Rev-erb to any DNA response element effectuates transcriptional modulation of genes such as, for example, Apo-C, and that such a finding can be used to develop methods for screening compounds that are useful in the treatment of a lipid metabolism dysfunction associated with apolipoprotein C-III. In the preferred embodiments, Trueheart expressly teaches that the methods are applicable for screening of compounds which change the activity of G-protein coupled receptors or EPH receptors. Trueheart discloses more than 60 species of such GPCRs (e.g., α_{1A}-adrenergic receptor, α_{1B}-adrenergic receptor, α_2-adrenergic receptor, α_{2B}-adrenergic receptor, α_1-adrenergic receptor, β-adrenergic receptor, β_3-adrenergic receptor, etc) and more than 30 species of "preferred EPH receptors." See, the SUMMARY OF THE INVENTION section of USP '705. In the "Screening and Selection" section VI, Trueheart contemplates that such screening methods may comprise measurement of "GTPase activity, phospholipid hydrolysis, or protein phosphorylation patterns or enzyme activity." There is no mention of transcriptional modulation as claimed herein. The skilled worker is not motivated to use precisely the hRev-erb proteins in combination with any of the response elements taught by the cited secondary reference. Without such motivation, there can be no obviousness. *In re Baird*, 16 F.2d 380 (Fed.Cir. 1994).

Furthermore, it is now well-established that obviousness requires a suggestion of all the elements in a claim (*CFMT Inc., v Yieldup Int'l Corp.* 349 F.3d 1333, 1342 [68 USPQ2d 1940] (Fed. Cir. 2003)) and requires a reason that would have prompted [a skilled worker] to combine the elements in the way the claimed new invention does (*Ex parte Alexander* (Decided November 30, 2007; *86 USPQ2d 1120*)). Nothing in the teachings of the '705 patent and/or the Harding publication would motivate a skilled worker to utilize the claimed components for the specific purpose claimed herein, i.e., screening a compound that is useful in the treatment lipid metabolism

dysfunction, as presently claimed. Absent such, Trueheart in combination with Harding cannot render obvious the subject matter of the present claims. Withdrawal of the rejection is respectfully requested.

Dependent claims

With respect to the other dependent claims at issue, Applicants will not burden the record with a discussion of same since they merely add to the unobviousness of claim 1 over the cited Trueheart and Harding references. However, Applicants reserve the right to provide rebuttals against the statements in the Office Action vis-à-vis the dependent claim, at a later date, if ever necessary.

Withdrawal of the rejection is respectfully requested.

In the absence of a more pertinent reference, it appears that the application is now in condition for allowance, but if there are any residual issues, the Examiner is courteously invited to telephone Counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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